

REMARKS AND REASONING

Status of the Claims

Claims 10, 12, 13, and 28 are rejected. Upon entry of the instant amendment, Claims 10 and 28 are amended, and Claims 28-34 are new.

Support for these amendments is found in the claims as originally filed and throughout the specification; for example, paragraphs [0094], [0101], [0112], [0133], and [0218]-[0234].

Claim Rejection 35 USC § 112, Enablement

Claims 10, 12, 13, and 28 are rejected as allegedly failing to satisfy the requirements of 35 USC § 112, enablement.

The instant invention is directed, in part, to a diagnostic assay. The claimed diagnostic assay entails detecting mRNA profiles in saliva supernatant from a subject and comparing the subject's mRNA profile to a predetermined human mRNA profile.

The instant invention further provides that mRNA profile is derived from transcripts of IL8, DUSP1, H3F3A, OAZ1, S100P, IL1b, and SAT.

In assessing enablement of claims directed to diagnostic assays, the following guidelines are provided:

“[T]he term diagnostic assay is to be construed to mean any assay that can be used to help diagnose a condition, as opposed to any assay that can, in and of itself, diagnose a condition. A diagnosis is typically made by evaluating the results of several screening assays, each of which has some level of false results and, accordingly, each of the screening assays would be a diagnostic assay. Therefore, to enable a diagnostic assay use, a disclosure merely needs to teach how to make and use the assay for screening purposes.” TRAINING MATERIALS FOR EXAMINING PATENT APPLICATIONS WITH RESPECT TO 35 USC SECTION 112, FIRST PARAGRAPH ENABLEMENT OF CHEMICAL/BIOTECHNICAL APPLICATIONS, <http://www.uspto.gov/patents/law/lpecba.jsp#iia2>.

Applicants maintain that the invention is enabled in so much as it is directed to a diagnostic assay.

The Examiner states “that the instant claims are not interpreted as a diagnostic assay [but] a method for diagnosing a disease,” and thereby evades Applicants enablement reasoning and the recited guidelines and presumed enablement. Yet, contrary to the Examiner’s position, the instant claims follow the recognized form of a diagnostic assay claim.

For example, in *Ex parte Goldgaber*, the Board of Patent Appeals and Interferences identified claims directed to methods of detecting individuals possessing a particular nucleotide sequence as a “diagnostic assay.” 41 USPQ2d 1172, 1175 (BPAI 1995). Further examples of claimed diagnostic assays are provided in *Ex parte Arabshahi* (BPAI Appeal 2008-3325) and *Ex parte Valkirs* (BPAI Appeal 2007-0628).

While neither *Ex parte Arabshahi* nor *Ex parte Valkirs* is precedential, Applicants do not rely on any legal conclusions reached by the Board in these appeals, but the descriptions of the claims as diagnostic assays.

Based on these examples, Applicants maintain that enablement of the instant claims is to be judged based on the guidelines for diagnostic assays; that is, “to enable a diagnostic assay use, a disclosure merely needs to teach how to make and use the assay for screening purposes.”

The Examiner finds that the specification is enabled for a method of screening gene expression in saliva. Office Action (dated June 8, 2011), page 3, third paragraph. The training materials provide that a claimed diagnostic assay is enabled if the inventor teaches how to make and use the assay for screening purposes. Accordingly, the instant claims are enabled.

Therefore, the rejection of the instant claims as lacking enablement should be withdrawn.

Claim Rejection 35 USC § 103

Claims 10, 12, 13, and 28 are rejected as obvious in light of Kopreski (US6,607,898), Kopreski (US6,759,217), and Squire *et al.* (2002) Head and Neck 24:874-887.

The instant claims are drawn, in part, to a diagnostic assay based on the comparison of an mRNA profile from a subject with that of a predetermined mRNA profile. The Applicants have identified IL8 as a diagnostic marker.

When rejecting claims under 35 U.S.C. § 103, the Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. MPEP 2142. A rationale to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination yielded nothing more than predictable results. *KSR International v. Teleflex Inc.*, 82 USPQ2d 1385 (2007). If any of these findings cannot be made, then this rationale cannot be used to support a conclusion of obviousness. MPEP 2143A.

The Examiner alleges, in supporting a *prima facie* case of obviousness, that when combined the Kopreski patents teach a method for diagnosing cancer by detecting hTR, hTERT, EGF, c-myc, and her-2/neu mRNA in saliva. Further, the Kopreski patents teach using quantitative PCR. As the Examiner readily admits, neither Kopreski patent teaches or suggests that cancer of the oral cavity can be detected by the described methods or the use of IL8. For this the Examiner relies on Squire.

The Examiner alleges that Squire teaches that intracellular IL8 mRNA is increased in HNSCC cells.

Thus, when viewed in whole, the Examiner's allegation of obviousness is that one skilled in the art would combine the methods of detecting cancer taught by Kopreski with the observed increased intracellular IL8 mRNA in HNSCC cells taught by Squire to arrive at the instant invention with predictable results.

As Applicants previously pointed out to the Examiner, the flaw in the Examiner's reasoning is that none of the cited references teach or suggest that the expression profile observed in the cellular fractions studied by Squire would correlate to the expression profile in saliva supernatant. Thus, absent from the cited art is any suggestion that observations made concerning intracellular mRNA is at all relevant to the detection of mRNA extracellularly. And because of this absence, the Examiner's conclusion of obviousness fails.

Applicants reasoning is supported by *Ex parte Valkirs*, discussed above.

In *Ex parte Valkirs* the Board considered claims to a combination of biomarkers used in a diagnostic assay for stroke or cerebral injury. In rejecting the claims as obvious, the examiner in

Ex parte Valkirs, like the Examiner here with Squire, cited a publication which taught that the claimed marker was detectable intracellularly. From this, the examiner in *Ex parte Valkirs* urged, like here, that because the marker was found intracellularly, one of skill would have recognized that the marker would also be present in the extracellular milieu surrounding the cell. The Board rejected this line of reasoning.

The Board found that the ability to detect a biomarker in a cell does not suggest to one of skill that this same biomarker will also be found in the extracellular milieu with another biomarker. Relying in part on this reasoning, the Board reversed the Examiner's obviousness rejection.

Applying the Board's reasoning to the instant claims, one of skill would not reasonably expect that the presence of intracellular IL8 transcripts in HNSCC cells would mean that this same transcript would be present in the extracellular milieu. Moreover, even if IL8 were detectable in the extracellular milieu, there is no reasonable expectation that intracellular expression levels of IL8 in HNSCC cells would correlate with the levels found in the extracellular milieu; for example, saliva supernatant.

Therefore, Applicants maintain that the instant claims are not rendered obvious in light of the cited art, in part, because prior the instant application it was unpredictable whether extracellular IL8 levels in saliva could be correlated with OSCC.

Accordingly, Applicants maintain that the rejection of the instant claims on the basis of obviousness should be withdrawn.

CONCLUSION

All the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections.

Applicant believes that a full and complete reply has been made to the outstanding Office Action, and as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided below.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any necessary fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17, which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310 (Docket Reference: 008074-5002-US).

Respectfully submitted,

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